

9-28-77

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: 8/29/77

SUBJECT: Re-evaluation of rejected minor use tolerances petitions involving Chlorothalonil

FROM: Robert Coberly, Tox. Branch

Robert Coberly 9/20/77

TO: Mr. Charles L. Smith
Special Registration Branch

Thru: Dr. O.E. Paynter
Chief, Toxicology Branch

E. J. Cooper 9/28/77

Thru: Dr. Martin Rogoff
Pesticide Science Officer

Pesticide Petition No: 6E 1841

Petitioner: Dr. C.C. Compton
IR-4 Project Coordinator
New Jersey Agricultural Experiment Station
Box 231, Cook College, Rutgers

Request: Conduct a re-evaluation of the IR-4 minor use petition on which I recommended against the establishment of the requested tolerance. See R. Coberly memo to Patricia Critchlow of 1/27/77.

Recommendation: The toxicological data submitted in prior petitions for support of various tolerances have been totally applied to this IR-4 request for tolerances on minor crops. The resulting conclusions fall into the following two areas:

- 1) The requested tolerances in or on turnip greens, chicory, and mustard greens will not contribute a significant increase of the chemical in the daily human diet. Ergo, no undue human health hazards will be created.
- 2) The requested tolerance in or on escarole will contribute a calculated amount of the chemical into the daily diet sufficient to reduce the normal 100 fold safety factor to approximately 89. This reduction in the human safety factor would place the requested human health assessment into the realm of conjecture.

Related Petitions: 7G0516, 7F0599, 9F0743, 1F1024, 2F1230, 3F1382, 4F1502, 5E1569, 6F1749, 6E1761, 6H5136, 6G1813, and 6E1841.

Existing Tolerances: §180.275

15 ppm in or on celery

5 ppm in or on broccoli, brussels sprouts, cabbage, cauliflower, cucumbers, melons, onions (green), pumpkins, snap beans, squash (summer and winter) and tomatoes.

3.0 ppm in or on passion fruit

1.0 ppm in or on carrots and sweet corn (kernels plus cob with husks removed).

0.5 ppm in or on onions (dry bulb).

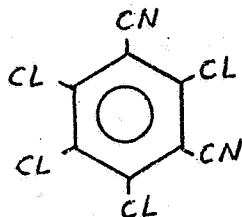
0.3 ppm in or on peanuts

0.1 ppm in or on potatoes

Chemical Name: 2,4,5,6-tetrachloroisophthalonitrile

Synonyms: Daconil, DAC-2787, Forturf

Structure:



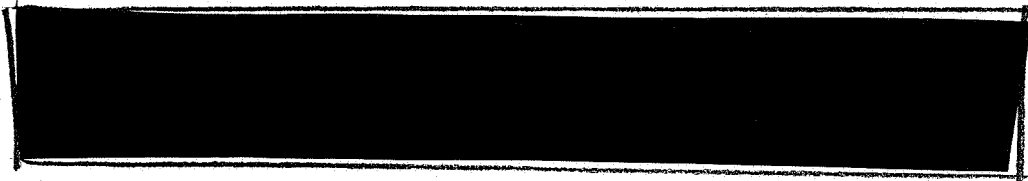
Use: Fungicide

Formulation: Bravo 6F EPA #677-313

Active Ingredient

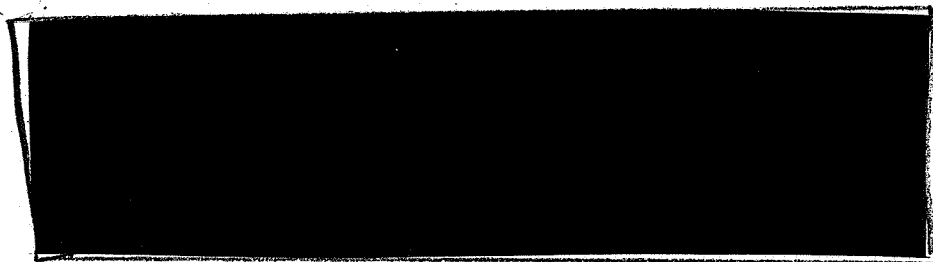
54.00% chlorothalonil

Inert Ingredients



INERT INGREDIENT INFORMATION IS NOT INCLUDED

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*cleared under 40 CFR 180.1001(c)

Letter of authorization: 3/17/76 memo from J.R. Lucietta to Drew McBaker, Jr.

Background Information

Following is a brief summary listing of the numerous toxicological reviews conducted on the diversified toxicity submitted by the registrant to support the safety of his requested tolerances on food and feed: No studies were conducted at IBT.

acute rat oral LD50 (PP# 1F1024)	> 10,000 mg/kg
acute dog oral LD50 (PP# 1F1024)	> 5,000 mg/kg
acute rabbit dermal LD50 (PP# 1F1024)	> 10,000 mg/kg
rabbit eye irritation (PP# 1F1024)	transient irritation
acute rabbit inhalation LC50 (PP# 1F1024)	> 4.7 mg/L
rabbit teratogenic (PP# 9F0743)	negative at 62.5 mg/kg (highest fed level)
16 week Dog Feeding	NEL < 250 ppm
4 month Rat Feeding (#200-198)	NEL < 250 ppm
2 Year Dog Feeding	NEL < 0.15%
2 Year Dog Feeding (#200-206)	NEL 60 ppm
2 Year Rat Feeding (#200-154)	NEL < 0.5%
18 Month Rat Feeding (#200-175)	NEL < 0.05%
2 Year Rat Feeding (#200-205)	NEL 60 ppm
3 Generation Rat Reproduction (#200-155)	NEL < 0.5%
3 Generation Rat Reproduction (#200-150)	NEL 15,000 ppm (reproduction)
	NEL 1,500 ppm (lactation)

Metabolite Data (DAC -3701-14-hydroxy-2,5,6-trichloroisophthalonitrile)

Acute Rat Oral LD50 (S-D Rats)	male 422 mg/kg female 242 mg/kg
Acute Dog Oral LD50 PP # 2F1230 (293-021)	100 mg/kg
Acute Rat Oral LD50 PP # 2F1230 (293-004)	332 mg/kg
14 month Rat Feeding PP # 2F1230 (#24-051)	NEL 100 ppm
90 Day Dog Feeding PP # 2F1230 (#24-052)	NEL < 50 ppm
3 Generation Rat Reproduction PP # 2F1230	NEL Not established

Host-Mediated Assay PP # 6F1799 (99% pure): negative

In Vivo Cytogenetic In Mice PP # 6F1799 (99% pure): *NEGATIVE*
MICE DOMINANT LETHAL TEST PP# 6F1799 (99% pure): A SIGNIFICANT INCREASE IN
EARLY DEATHS AT WEEK 3 OF MATING (SPERMATID STAGE) WAS
NOTED AT 6.5 mg/kg/day.

Mice Dominant Lethal Test PP # 6F1799 (99% pure): incomplete data provided.

Rat Dominant Lethal Test PP # 6F1799: negative at 8 mg/kg (5 daily oral doses) and at a single dose of 8 mg/kg (99% pure) (Lab # 24-101).

Rabbit Teratology (Lab # 293-032a) (PP # 6F1799): negative at 5.0 mg/kg/day

73 Week Rat Feeding (Lab #8180-70) (PP # 6F1799) (99% pure): NEL >200ppm
study does not satisfy the oncogenic protocol due to length of study.

Three Generation Rat Reproduction (PP # 6F1799) (99% pure): study is considered invalid due to numerous conflicting data, poor reporting, missing data and etc. Dr. Budny of Diamond Shamrock Chemical Co. agreed to this classification.

It was revealed during the Jan. 12, 1977 R. Coberly review of Pesticide Petition No. 6F1799 that the previously listed NEL of 120 ppm in the dog had been downgraded by Dr. E. Long to 60 ppm due to questionable effects at 120 ppm. Accordingly, the ADI was lowered from 0.03 mg/kg to 0.015 mg/kg and the MPI to 0.9 mg/day/60kg man. It was also pointed out in this review that the existing tolerances will contribute residues to the diet equal to the allowable daily intake (ADI) and also that a data gap exist which consist of a second oncogenic study. On the basis of these findings, establishment of the tolerance in or on soybeans was not recommended. Toxicology also recommended against establishing any of the pending tolerances (see memo of 1/27/77 from R. Coberly to Patricia Critchlow).

Present Action

On or about August 11, 1977 I was asked to re-review my position on cholorothalonil with respect to using the "common sense" approach as outlined in the May 1977 memo from Mr. Edwin L. Johnson, Deputy Assistant Administrator for Pesticide Programs to Acting Director, Registration Division. In this memo Mr. Edwin L. Johnson states, "Certainly, chemicals should not be extended, but in the absence of adverse data, a decision is to be made on the basis of available data for such uses, assessing the marginal value of the additional information now or at a future date. So long as we explain the basis for such decision per my instructions of February tolerance memo and these actions can be made on the merits and not on a "checklist" basis."

In following this directive, I offer the following comments:

- 1) Turnip greens is considered a minor crop which will not contribute a significant amount of residue to the human diet at a tolerance level of 15 ppm.
- 2) Chicory and Endive are considered minor crops which will not contribute a significant amount of residue to the human diet at a tolerance level of 6 ppm.
- 3) Mustard greens is considered a minor crop which will contribute a calculated amount of 0.016 mg to the daily human diet at the proposed tolerance of 15 ppm or 0.026 mg/day at 25 ppm (as requested by chemistry review of 10/3/76 by William S. Cox).
- 4) Escarole is listed in combination with lettuce in the "The Annual Per Capita Consumption of Selected Items of Food In the United States" by A.J.L. The percent of the diet for this combination is 1.15%. According to past procedures, this value is applied to escarole. Ergo, the contribution to the diet is 0.1 mg/day. Neither of these values permits the classification of escarole as a minor crop. If the tolerance is increased to 25 ppm, as requested by Chemistry Branch, the residue in the diet will increase to 0.43 mg/day or approximately 47% of the MPI.

- 5) The existing data consists of a variety of toxicity data including a chronic feeding and oncogenic study which supports a no effect level.
- 6) The 100 fold human safety factor used to establish the ADI will not be statistically significantly reduced if the IR-4 request for tolerances in turnip greens, chicory, and endive were to be established at 25 ppm (as recommended by Chemistry Branch).
- 7) The 100 fold human safety factor used to establish the ADI will be reduced to approximately 98.3 if the IR-4 request for tolerances in mustard greens at 15 ppm is granted. If the tolerance of 25 ppm is used the human safety factor would be reduced to approximately 97.4.
- 8) The 100 fold human safety factor used to establish the ADI will be reduced to approximately 89 if the requested tolerance of 6 ppm is established on escarole. If the tolerance of 25 ppm (recommended by Chemistry Branch) is established, the human safety factor will be reduced to approximately 53.
- 9) There is a two fold difference between the dog no effect level (60 ppm) and the dog lowest effect level (120 ppm).
- 10) The second oncogenic study will be supplied by Diamond Shamrock as per conference with Dr. Budny at el on 8/8/77.